TRANSCRIPTOMIC SIGNATURES CLASSIFYING CHO QUASISPECIES

Ankita Singh, Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark
Helene F. Kildegaard, Novo Nordisk Foundation Center for Biosustainability
Mikael R. Andersen, Technical University of Denmark

Chinese hamster ovary (CHO) cell lines have the capacity to correctly fold, assemble and modify proteins post-translationally, and consequently is commonly used expression systems for recombinant therapeutic proteins. In recent years, a thorough understanding of process parameters of individual CHO cell lines have been achieved, but comprehending the genomic or pathway-specific distinction of various CHO cell lines at transcriptome level still remains a challenge. To address this challenge i.e. to gain cell line specific understanding of modulation in the pathways and gene sets, an RNA-seq study of CHOS, CHOK1 and DG44 cell lines grown in batch culture has been performed using an in-house developed pipeline. An R-based application was developed specifically for this CHO dataset to further calculate expression values across different cell lines. Furthermore, two main conditions have been defined to perform differential expression (DE) analysis to study regulatory activity across the cell lines. First, we performed a DE analysis of exponential and stationary phase of different cell lines where gene sets having significant DE ($p<0.05$) was identified. And the second one is DE comparison for both phases disjointedly and collectively over cell lines was conducted and genes with $p<0.05$ was identified. Among the identified up- and down-regulated genes, unique and common genes across phases and cell lines were identified. Additionally, specific pathways have been found to be regulated similarly across various cell lines and some to be transversely regulated over phases. We have thereby mapped the cell line-specific genetic regulation. This can be implemented in picking desired characters, across various CHO cell lines and in determining the structure of super CHO cell lines having the capability to combat most of the deficiencies exiting till today.